



Addiction to Nasal Decongestants Based on α-Adrenoceptor Agonists Case Series and Literature Review

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Abstract: Otorhinolaryngologists describe nasal obstruction as a common symptom, moreover a prolonged use of nasal decongestants based on α -adrenoceptor agonists lead to a vicious circle of addiction. This addiction is favoured by easy access to this variety of over-the-counter medications, which are often considered risk-free. The patient may experience a spectrum of mental disorders when deprived of the agent of his addiction, which can range from moderate discomfort to panic attacks or even hallucinations. In this article, we present an analysis of a series of cases of patients who chronically abuse nasal decongestants, and a review of the literature.

Keywords: "nasal decongestant"; "nasal obstruction"; "OTC"; "addiction"; "psychiatric disorders"

JEL Classification: Q01

1. Introduction

The word "addiction" has recently become so popular that it is used to describe several conditions other than those induced by pharmacological or chemical agents. ICD-11 defines substance abuse as "a regulation disorder of a psychoactive substance use resulting from repeated or continuous use of the substance". The central feature is a strong internal desire to use the substance, reflected in the inability to control its use, prioritizing consumption over other activities and the persistence of abuse despite the negative effects (Basu, 2018, pp. 54-62).

The widespread idea is that the addictive agent must have inherent pharmacological properties to induce physical dependence, to satisfy psychological needs and to generate a state of tolerance of the addict, all

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for the addiction to exist. Stecker stated in 1952 that "paradoxically, people can become addicted to certain drugs that do not have much more potent effect than water" (Strecker, 1952, p. 123).

The aim of this work was to analyse and demonstrate the potential of abusive self-administration of nasal decongestants based on α -adrenoceptor agonists, drugs erroneously considered harmless. Close inter-speciality ENT-Psychiatry collaboration is needed in the management of such cases, but also to improve the administration legislation of potentially addictive substances.

2. Case Series

2.1. Case 1

A 29-year-old male with no psychiatric history, a user for about 10 years of nasal decongestants. The initiation of decongestant drops begins following an acute upper respiratory tract infection, the drug being prescribed due to nasal obstruction. The patient relates a situation in which, at the end of a family reunion, his partner leaves the location with the patient's decongestant spray inside the bag. Being in the circumstance that he did not have easy access to a pharmacy, he describes an episode of anger, anxiety attack and suffocation sensation for a period of 15-20 minutes. Forced to travel a relatively long distance to purchase a decongestant spray, he stated that while driving the vehicle, "I felt like I was about to explode because of anger, I wanted to punch someone", and that the car was driven aggressively.

2.2. Case 2

An 18-year-old female with a history of anxiety depressive disorder, initiates a treatment with xylometazoline-based nasal decongestant spray, following an onset of allergic rhinitis. Even though the doctor mentioned the cessation of the spray after a maximum of 5 days of use, warning the patient that an addiction may occur, the patient continues to use it, reaching 21 days of administration. After stopping the xylometazoline administration, the bilateral nasal obstruction is established, rebellious to topical corticosteroids and nasal lavage with saline.

2.3. Case 3

A 37-year-old patient with no psychiatric history, with nasal obstruction under treatment with nasal decongestant spray. For the next 8 days, she administered about 12 spray bottles, because according to the patient "the symptoms subsided only for a short time". After 8 days of use, he suddenly stops the administration and his wife notices that the patient becomes anxious and agitated. At work, the patient reports that he feels excluded by an organized conspiracy by the colleagues, and during lunch he stated that the salad offered in the canteen should not be eaten because it could be poisoned. The patient becomes paranoid and confused. After creating a scene in which he accuses his colleagues of attempted murder by poisoning him, he was urgently hospitalized in a psychiatric unit. During the referral, the patient maintains his beliefs for 24 hours. A specialized treatment was instituted, along with the withdrawal of nasal decongestants. In 48 hours, the paranoid thoughts resolve.

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2.4. Case 4

A 42-year-old patient presents to the ENT clinic for chronic bilateral nasal obstruction. The clinical examination revealed rhino-sinus cavities and mucous membranes with physiological limits. The patient insisted on being hospitalized and investigated because she accused a strong pain in the visceral cranium, stating "It is as if my head could split in two. I am afraid for my life!". Suspecting a possible sphenoid sinusitis, the patient was hospitalized, and a brain CT scan was performed. It did not show any active pathological process of the cephalic extremity. Throughout the hospitalization (2 days) the patient administered 4 bottles of nasal decongestants, which she had purchased before presenting for investigation.

When asked about the frequency of use, she revealed that she has been using constantly for about 8 years and that she always has at least 2 bottles with her. When asked to give up her medicine, the patient becomes anxious and reports that "without the spray, she simply could not breathe" and that "she is afraid that she might die during her sleep". A series of nasal endoscopic images was recorded with rigid 0° scope to evaluate the nasal mucosa pre and post administration of nasal decongestants at regular time intervals as seen in Fig. 1. It shows how the effect on the nasal mucosa is well active even after 90 min so there was no need for repeat administrations, proving the fact that the abuse was not the result of tachyphylaxis, failure of the drug or other organic cause. A psychiatric consultation was requested.

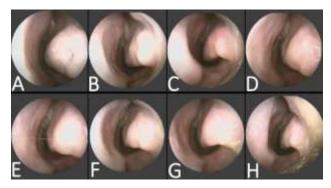


Figure 1. Evaluation of the Pharmacological Effects on the Nasal Mucosa of the Nasal Decongestants. A – Prior to Administration; Post Administration B at 3 min; C at 8 min; D at 15 min; E at 30 min; F at 45 min; G at 60 min; H at 90 min

Table 1. Patient Data

No.	Sex	Age	Patient psychiatr ic history	ENT condition prior to treatment with nasal decongestant	Psychiatric manifestations after stopping nasal decongestant administration	Duration Pharmacolo gical agent abuse
1.	M	29 years	NO	Acute upper respiratory tract infection	Anger rage, anxiety	10 years
2.	F	18 years	YES	Acute upper respiratory tract infection	Anxiety, depression	21 days
3.	M	37 years	NO	Acute rhinitis	Paranoid thoughts	16 days
4.	F	42 years	YES	Chronic rhinitis	Visual hallucinations	8 years

3. Literature Review

G. W. Blackwood et al. describe a case of a patient who suffered from a long-term personality disorder for over 7 months in the form of paranoid psychosis and delirium, secondary to chronic abuse of nasal decongestant spray based on oxymetazoline for several years. The spray improved the symptoms of chronic nasal obstruction, but the patient also reported a euphoric feeling for a few seconds after administration and that the decongestants help her cope better with daily life. She was treated with sedatives and anxiolytics for the first days after hospitalization, after which the symptoms were completely remitted (Blackwood, 1982, p. 27).

S. Snow et al. reports the case of a 27-year-old patient who was addicted to phenylephrine-based nasal drops for several years. She developed a psychosis after increasing the use of nasal spray. The patient used nasal decongestants during the day in both nostrils at about 15 minutes intervals.

Due to depression and suicidal ideation, the patient was hospitalized in a psychiatric unit. There were also recorded episodes of visual and tactile hallucinations, with the patient stating that there were snakes and insects crawling on her body. There were no abnormalities found at the neurological and clinical examination, CT, EEG, and spinal puncture. The clinical examination was within physiological limits, but increased values of blood pressure and oedema of the nasal-sinus mucosa were recorded. The patient complained of suffocation and shortness of breath when she stopped using her nasal decongestants, resorting to breathing through a wet handkerchief, possibly a new obsessive behaviour to replace the old one. All symptoms disappeared after the cessation of the medication (Snow, 1980, pp. 297-299).

Anand et al. documents a group of six prisoners who abused xylometazoline-based nasal drops. The method of administration they used was quite unusual. In a spoon, the detainees brought to the boiling point between 20-60 drops at a concentration of 0.1% and inhaled the vapours. Usually, the procedure was organized 3 times a day, the effects set in quickly and lasted at least 2-4 hours. During regular visits to the prison's ambulatory department, the detainees procured nasal decongestants, reporting false symptoms of rhinosinusitis and allergic reactions, to get the drops. The psychoactive effects of xylometazoline have been described as "stimulating", "exciting" and conferred a "feeling of power". There were no psychotic symptoms noted. The duration of the abuse was 3 years for 4 prisoners and 2



years for 2 detainees, the information was extracted from the medical registries of the unit. No detainee reported tachyphylaxis on the pleasant effects of xylometazoline vapor inhalation, and withdrawal symptoms included anxiety-depressive disorder and insomnia (Anand, 2008, pp. 2163–2168).

4. Discussions

In the prospective study led by S. Cartabuke et al. on paediatric patients undergoing various rhino-sinus procedures, the hemodynamic effects and systemic absorption of topically applied oxymetazoline were evaluated. In the routine practice of the ENT specialty, the surgeon places a toupee soaked in oxymetazoline (1.5 mL, 0.05% concentration) in the nostrils. Blood samples were collected at 5, 10, 20, 45, 90 and 150 minutes to titrate the circulating level of oxymetazoline. Hemodynamic data were recorded at 5-minute intervals.

Hemodynamic changes were clinically negligible, the bioavailability of oxymetazoline administered on the toupee was double the one of the sprays, but systemic absorption was extremely slow, contributing to low serum concentrations and low hemodynamic effects (Cartabuke, 2019, pp. 1-7).

Matsumaru et al. investigated the toxicity of an $\alpha 1L$ -adrenoceptor agonist ESR 1150 CL and compared the pharmacokinetic and toxicokinetic properties in a comparative study in monkeys and mice. Oral ESR 1150 CL was administered for four weeks, which increased blood pressure in mice, but the same effect could not be observed in monkeys in the toxicity study. Pharmacokinetic evaluation showed good absorption of the compound, but both species showed low serum levels, and therefore low bioavailability (Matsumaru, 2005, pp. 273-283).

We believe that addiction can be better understood by studying the characteristics of the patient's psyche dependent on the study of the pharmacological properties of the agents. Not all addictive substances cause tachyphylaxis or a state of physical dependence. Some patients maintained their dependence on nasal decongestants without increasing the dose of addictive agent. However, the patient seems to have a special psychological relationship, a pathological dependence on the pharmacological agent, without which he cannot cope with the stressors in his life.

This addiction subsequently produces a pathological desire, a key feature of all addictions that is reflected in the reorientation and adaptation of the addict's lifestyle, focused on the use of nasal decongestants. The first step of addiction occurs when the individual procures himself a drug that converts respiratory discomfort into relief or even pleasure, when his depression is replaced by a state of well-being. The patient's mind goes through an experience he cannot forget, a strong and sudden improvement of an unbearable previous condition, in our case, nasal obstruction. This sudden change in psychological dynamics from frustration to satisfaction produces a state of release of fear, in which security rules. This concept is illustrated by using a quasi-common expression to all addicts after the administration of the addictive agent: "now I am not afraid of anyone or anything, I can do whatever I want".

A common symptom, often described by otorhinolaryngologists, is nasal obstruction. When fixed anatomical obstructions are ruled out and the rhino-sinus examination is within physiological limits, intermittent oedema of the rhino-sinus mucosa is usually incriminated.



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Topical alpha-adrenergic decongestants activate in a wide range of over-the-counter drugs, and vasoconstriction is obtained by stimulating alpha-adrenergic receptors present in the blood vessels of the mucosa, is their main mechanism of action (Yoo, 1997, pp. 40-43).

Prolonged administration of decongestant drops leads to the development of reflex nasal congestion known as "drug induced rhinitis". To prevent this phenomenon, more precisely to treat nasal obstruction, the use of topical sympathomimetic decongestants is usually limited to 5 days (Hall, 1985, pp. 605-616).

Even though the appearance of addiction following the use nasal decongestant after a period of more than 5 days is clearly mentioned in the leaflet, obtaining this substance is still uncontrolled and easy for the public, making the psychic manifestations initiated by its withdrawal endanger the patient's life, and those around him (Belin, 2012).

ENT clinics are familiar with the cases of patients who use the initial prescription of nasal decongestants for therapeutic purposes, to continue their administration to satisfy the addiction. The physiological effect causes withdrawal of the medication and continuous reporting of nasal congestion may strengthen the clinical justification for continuing the treatment. It is often difficult to obtain an accurate history, not only because of false reports, but also because of the patient's belief that this usual medication is unable to cause any harm (Graf, 1996).

The author's opinion is that the most important psychological aspect of addiction is the patient's need to distort reality. A common manifestation of addiction is the idea of bodily dysfunction as in the case of the patient who was sure that without the drops, he could have suffocated and died. Another form of pathological ideation observed, common to all addicts is that when using the addictive agent, they feel stronger and can function better. This false increase in performance cannot be attributed to the drugs themselves. The addict is self-convinced in a strange and disappointing way that the drug gives him the feeling that he is in control, considering that he can cope with stress much more effectively.

5. Conclusions

The particularities of the cases presented in the study, corroborated with data from the high scientific literature, denote the increased potential for psychiatric disorders of varying intensity to psychosis, with behavioural manifestations dangerous to the life and health of the patient and close circle, because of administration abuse of nasal decongestants based on an adrenoceptor agonist, medicinal substances erroneously considered to be harmless.

Abuse and addiction of nasal decongestants is not always connected to organic nasal obstruction or failure of the pharmacological agent.

Even in increasingly larger doses effects of this class of drugs is not enough to cause systemic lifethreatening issues, but they may still cause addictive behaviours or trigger psychiatric disturbances. Further research is needed to shed light on these aspects.

All that is presented obliges us to a prompt and complex response, by reviewing the therapeutic protocols and improving the control of the administration of this class of substances. The group of authors comes with a proposal of inclusion of these substances in a category that implies strict release based on the doctor's prescription.

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